Medical Coverage Policy

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Helicobacter Pylori Serology Testing

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INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses serology testing in the adult and pediatric populations for Helicobacter pylori infection which is associated with peptic ulcer disease and gastric cancer.

Coverage Policy

Serology/antibody testing (CPT code 86677) for diagnosing Helicobacter pylori is considered experimental, investigational and unproven for ANY indication including making a diagnosis of a Helicobacter pylori infection.

General Background

Helicobacter pylori (H. pylori) is a key causal factor in most peptic ulcer disease and a primary risk factor for gastric cancer. The pathogenic role of H. pylori in peptic ulcer disease, both duodenal and gastric, is well recognized. Nearly 95% of patients with duodenal ulcers and 80% of patients with gastric ulcers are found to be infected with H. pylori. Treatment for H. pylori infection includes varied combinations of antibiotics, proton pump

inhibitors (PPIs), histamine H2 receptor antagonists and bismuth compounds. Eradication of H. pylori significantly lowers the recurrence rate of H. pylori-associated peptic ulcers.

It is estimated that approximately 13–81% of people have an infection with H. pylori and prevalence varies with age, region, race, and socioeconomic class (Best, et al., 2018). In a 2022 systematic review and retrospective study on racial disparities on H. pylori infection in the United States, Brown et al. found that Blacks and Hispanics had a higher infection prevalence rate compared to whites. The ratio of Black to white infection prevalence ranged from 1.3 to 5.4 and Hispanic to white ranged from 1.8 to 4.4. Compared to whites, Blacks were found to have 2.6–4.4 increased odds of having an infection and Hispanics were found to have 1.8–3.9 increased odds of having an infection. According to the authors, this study points to a need for better understanding of the racial differences in H. pylori infection prevalence which may lead to improved risk stratification strategies for gastric cancer prevention.

H. Pylori Testing Methods

H. pylori infection can be confirmed by invasive or noninvasive methods. Invasive tests require upper esophagogastroduodenal (EGD) endoscopy, which is considered the reference method of diagnosis. During endoscopy, biopsy specimens of the stomach and duodenum are obtained, and the diagnosis of H. pylori can be made by rapid urease testing (RUT), histology and/or culture. If possible, noninvasive testing is done before tissue testing. Noninvasive methods include urea breath testing (UBT), stool antigen testing (e.g. H. pylori stool antigen [HpSA]) and serology. The clinical utility of these testing methods lies in their ability to accurately identify H. pylori infection, which allows for subsequent treatment and eradication. Urea breath testing has been proven to be a safe and effective test for identifying the presence of H. pylori with a reported sensitivity of 94.7% and specificity 95.7% (Vakil and Fendrick, 2005). The accuracy of UBT is comparable to endoscopic biopsy (Islam, et al., 2005; Perri, et al., 2005). Sensitivity and specificity ranges of 90%–93% and 91%–100% respectively, have been reported for stool antigen testing (Canadian Agency for Drugs and Technologies in Health [CADTH], 2015).

Best et al. (2018) conducted a Cochrane systematic review of the literature to compare the diagnostic accuracy of non-invasive H. pylori testing in symptomatic and non-symptomatic people. The diagnostic tests included urea breath testing, serology and stool antigen testing. A total of 101 prospective and retrospective studies met inclusion criteria. Of the 11,003 subjects, 5839 had H pylori. The studies evaluated the tests when done alone or in combination. A total of 34 studies (n=4242) evaluated serology; 29 studies (n=2988) evaluated stool antigen test; 34 studies (n=3139) evaluated urea breath test-13C; 21 studies (n=1810) evaluated urea breath test-14C; and two studies (n=127) evaluated urea breath test. There was a statistically significant difference in the diagnostic accuracy between urea breath test-13C, urea breath test 14C, serology and stool antigen test (p=0.024). Specificity of urea breath test-13C, 14C, serology and stool antigen test was 0.94, 0.92, 0.84 and 0.83 respectively. The author's concluded that in symptomatic populations with no history of gastrectomy, and no recent use of proton pump inhibitors or antibiotics, urea breath tests had a high diagnostic accuracy, whereas serology and stool antigen tests had lower accuracy to diagnose H. pylori. The thresholds used for these tests were highly variable and the authors were unable to identify specific thresholds that might be useful in clinical practice. There is a need for additional high quality studies to assess the accuracy of non-invasive tests for H. pylori.

Serological assays measure specific H. pylori immunoglobulin G (IgG) antibodies that determine if an individual has been infected. Serological testing has been the mainstay of H. pylori diagnosis, particularly in primary care, due to the accessibility, rapid results and low cost of this testing method. However, some serological tests have not been locally validated and therefore have suboptimal sensitivity and specificity in practice. The value of noninvasive H. pylori testing is also related to the background prevalence of H. pylori infection. False-positives are more likely to occur in areas where H. pylori infections are less prevalent (Talley, et al., 2005a). Serological tests are also unreliable indicators of H. pylori status in patients who have received treatment for the infection. Because it cannot distinguish between current and past infection, serological testing has poor accuracy in settings of low and intermediate H. pylori prevalence, limiting its value in the United States (Vakil and Fendrick, 2005).

Serology testing for H. pylori pre-dates UBT and stool antigen testing, and has been reported to have decreased accuracy based on local validation with a wider sensitivity and specificity range of 80–95%. Since the positive predictive value of antibody testing is influenced by the prevalence of an infection, the PPV in areas of low

prevalence such as much of the United States is poor. A positive test has little value in predicting the actual presence of an active infection. False-positives lead to inappropriate treatment, as well as lack of treatment response and encouragement of antibiotic resistance (Vakil and Fendrick, 2005). The low accuracy of serology testing results in the need for additional confirmatory non-invasive (i.e., UBT, stool antigen), or invasive (i.e., endoscopy/biopsy) testing. Therefore the performance and clinical utility of this testing method compared to other non-invasive methods is lacking.

Professional Societies/Organizations
American College of Gastroenterology (ACG): According to the ACG practice guidelines for the management of H. pylori infection, antibody testing (e.g., serum, whole blood, urine) is widely available but has poor positive predictive value in populations with a low prevalence of H. pylori infection, limiting its usefulness in clinical practice. Antibody testing is of limited benefit in documenting eradication of H. pylori, as results can remain positive years after successful cure of the infection (Chey, et al., 2007). Testing to prove H. pylori eradication should be performed using a urea breath test, fecal antigen test or biopsy-based testing at least four weeks after the completion of antibiotic therapy and 1–2 weeks after PPI therapy has been withheld. The ACG noted that "because of the higher pretest probability of infection, patients with documented PUD represent a rare group, where it is acceptable to utilize an IgG H. pylori antibody test." In most other scenarios in which the pretest probability of infection is lower, tests which identify active disease are preferred over antibody testing (Chey, et al., 2017).

The American Board of Internal Medicine's (ABIM) Foundation Choosing Wisely® Initiative: A Choosing Wisely statement from American Society for Clinical Pathology (2016) stated "serologic evaluation of patients to determine the presence/absence of Helicobacter pylori (H. pylori) infection is no longer considered clinically useful. Alternative noninvasive testing methods (e.g., the urea breath test and stool antigen test) exist for detecting the presence of the bacteria and have demonstrated higher clinical utility, sensitivity, and specificity".

Use Outside of the US
In a guideline on Helicobacter pylori, the World Gastroenterology Organization stated that, "Serological antibody tests are commonly available. Although they are useful as seroepidemiological surveys, these tests often lack the sensitivity and specificity required for decision-making in individual patients and are generally not very helpful. They need to be validated for specific locations, and the issue of false results due to cross-reactivity has rarely been addressed. In a community with moderate H. pylori prevalence, the accuracy of these tests may not exceed 50% (Katelaris, et al., 2021)." This position was reaffirmed in the 2023 update to the guideline (Katelaris, et al., 2023).

The H. pylori trends in Ireland indicated eradication rates were decreasing and the prevalence of antibiotic resistant bacteria was rising. Due to this trend, a working group was established to provide updated recommendations for the treatment of H. pylori. Experts in Ireland and Europe were included in the formation of the workgroup and divided into three groups to address diagnosis, treatment, and rescue therapy for H. pylori. The following are recommendations that pertain to the diagnosis of H. pylori (Smith, et al., 2017):

1. All adults with upper gastrointestinal symptoms should be tested for H. pylori.
2. The urea breath test is the standard noninvasive test for H. pylori diagnosis when available.
3. A locally validated stool antigen test may be used if accredited by the Irish National Accreditation.
4. Invasive testing involves endoscopy with combination histology taken from antrum and corpus combined with a rapid urea test.
5. PPI's should be stopped 14 days prior to testing.
6. Urea breath testing can be used for post eradication testing at least four weeks after therapy completion.

The European Helicobacter Study Group (EHSG) promotes multidisciplinary research and organizes consensus conferences to explore issues surrounding H. pylori infection. The Fifth Maastricht/Florence Consensus Conference included 43 experts from 24 countries who issued the following recommendations regarding diagnosis of H. pylori (Malfertheiner, et al., 2017):

1. The 13C-urea breath test (UBT) is recommended for the diagnosis of H. pylori infection. However a monoclonal stool antigen test (SAT) may be used as it has a high sensitivity and specificity.

2. Rapid serology testing has not been validated and is not recommended.
3. PPI's should be stopped at least two weeks prior to testing.
4. Antibiotics and bismuth compounds should be stopped at least four weeks prior to testing.
5. When there is an indication for endoscopy, the first line diagnostic test is the rapid urease test (RUT).
6. Serological testing for H. pylori infection may be used when results are locally validated.
7. UBT can be used to confirm H. pylori eradication.

Joint evidence-based guidelines from the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) include the following regarding H. pylori testing methods (Jones, et al., 2016):

1. PPI's should be stopped at least 2 weeks prior to H. pylori testing.
2. Antibiotics should be stopped four weeks prior to H. pylori testing.
3. The initial diagnosis of H. pylori should be done by upper gastrointestinal endoscopy with testing of gastric biopsies.
4. The initial diagnosis of H. Pylori should not be based on non-invasive tests (i.e., 13C urea breath test or H. pylori stool antigen test).
5. Tests based on the detection of antibodies (IgG, IgA) for H. pylori in serum, whole blood, urine, and saliva are not reliable for use in the clinical setting.
6. Testing the outcome of treatment should be performed at least four weeks after completion of therapy using the 13C-urea breath test or the two-step monoclonal stool H. pylori antigen test.

Italian guidelines published by Zagaria et al (2015) state that the H. Pylori test-and-treat strategy is appropriate for the initial management of uninvestigated dyspepsia as H. Pylori prevalence in adults in Italy is over 20%. This approach is applicable to patients younger than 50 years without alarm symptoms. All dyspeptic patients older than 50 years or with alarm signs or symptoms should be referred for upper endoscopy. The guidelines further stated that when the test-and-treat strategy is applied, an accurate diagnosis is mandatory using a non-invasive test, either the C-urea breath test (UBT) or the monoclonal stool antigen test (SAT). These testing methods have shown high diagnostic accuracy in both the pre- and post-HP treatment setting (Zagaria, et al., 2015).

The National Institute for Health and Care Excellence (NICE) guidelines for the management of gastroesophageal reflux disease and dyspepsia in adults stated that H. pylori can be initially detected using either a carbon-13 urea breath test (UBT), stool antigen test or laboratory-based serology where its performance has been locally validated. Re-testing for H. pylori should be performed using a carbon-13 UBT, as there is currently insufficient evidence to recommend the stool antigen test as a test of eradication. NICE does not recommend the use office-based serological tests for H. pylori because of inadequate performance (NICE, 2014; updated 2019).

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD		No National Coverage Determination found	
LCD		No Local Coverage Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
86677	Antibody; Helicobacter pylori

ICD-10-CM Diagnosis Codes	Description
	All codes

***Current Procedural Terminology (CPT®) ©2022 American Medical Association: Chicago, IL.**

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